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Trimethoprim-sulphamethoxazole in gonorrhoea
A comparison with pivampicillin combined with probenecid

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A number of recent studies have shown the efficacy of sulphamethoxazole combined with trimethoprim (T-S) in uncomplicated gonorrhoea (Csonka, 1969; Kvorning, 1969; Carroll and Nicol, 1970; Ullman Niordson, and Zachariae, 1971; Evans, Churcher, and Human, 1972; Rodin and Seth, 1972; Svindland, 1973).

In most cases T-S has been given over several days. In venereology it may be desirable to have a one-day treatment. The present paper reports on a comparison between T-S and pivampicillin combined with probencid (P-P) both administered in 1-day schedules. The study includes an evaluation of the efficacy of these drugs in gonococcal pharyngeal infection.

Material and methods

During 1973 every man and woman attending the outpatient clinic of venereology, Marselisborg Hospital, Aarhus, and suffering from uncomplicated gonorrhoea was studied. The diagnosis of gonorrhoea was made by smear and culture but only culture-proven cases were included in the trial. The cultures were performed at the regional department of the Statens Seruminstitut. Selective medium was used as a routine. An immunofluorescence technique was used for identification in the case of genital specimens. Gonococci in non-genital specimens were identified on the basis of colonial and microscopical appearance and oxidase and sugar fermentation reactions.

Every second month the patients were treated with T-S in two doses with an 8-hr interval, each dose consisting of sulphamethoxazole 2 g. and trimethoprim 400 mg. The first dose of five tablets was taken under supervision in the clinic. Pregnant women and patients with a history of drug reaction to sulphonamides were excluded. T-S was used in 419 patients (235 men and 184 women). Every other month the treatment used was pivampicillin 1·4 g. combined with probenecid 1 g. (P-P). Patients with a history of adverse reactions to penicillin and those in whose cases incubating syphilis had to be ruled out were excluded from this group. P-P was given to 319 patients (156 men and 163 women), the whole dosage being taken under supervision in the clinic. All drugs were administered with 100 ml. water and between meals.

After treatment the patients were examined at weekly intervals and were considered to be cured if two consecutive cultures were negative. In women, cervical, urethral and rectal specimens were taken routinely. In pharyngeal infections, three negative cultures were required. Treatment failure was diagnosed in the cases of those recurrences in which sexual contact during the follow-up period was denied by the patient.

Results

The results of treatment are shown in Table I. The failure rate in the T-S group was 1·9 per cent. and in the P-P group 0·9 per cent. The difference between the two groups is not statistically significant ($P > 0{\cdot}1$). Futhermore, in two of the treatment failures in the T-S group, the patients admitted having failed to take the second dose. 1·2 per cent. in the T-S group and 4·4 per cent. in the P-P group did not return for follow-up.

Rectal gonorrhoea was found in 53 women (29 per cent.) in the T-S group and in fifty women (31 per cent.) in the P-P group. There were no treatment failures in these cases.

22 patients were treated for gonococcal pharyngeal infection (3 per cent.). Nine received T-S and all were cured. Thirteen received P-P and in this group there were two failures. One man in each group developed gonococcal epididymitis after one negative post-treatment culture.

In the T-S group, eight cases of post-gonococcal urethritis were recorded (3·4 per cent.), while in the P-P group twelve cases (7·7 per cent.) were found. The difference is not statistically significant ($0{\cdot}1 > P > 0{\cdot}05$).

SIDE-EFFECTS

These are shown in Table II. Four patients treated with T-S and one patient on P-P developed a rash after treatment.

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TABLE I *Results of treatment*

Treatment	*Results*	*No. of patients*			
		Males	*Females*	*Total*	
				No.	*Per cent.*
Sulphamethoxazole-trimethoprim (T-S)	Cure	214	176	390	93·1
	Re-infection	11	5	16	3·8
	Treatment failure	7	1	8	1·9
	No follow-up	3	2	5	1·2
	Total	235	184	419	100·0
Pivampicillin-probenecid (P-P)	Cure	140	153	293	91·9
	Re-infection	7	2	9	2·8
	Treatment failure	3	0	3	0·9
	No follow-up	6	8	14	4·4
	Total	156	163	319	100·0

TABLE II *Side-effects*

Treatment	*T-S* (419)	*P-P* (319)
Dyspepsia	2	6
Rash	4 (1 per cent.)	1 (0·3 per cent.)

Discussion

Treatment with T-S seems to be highly effective in uncomplicated gonorrhoea. The results of the 1-day treatment in this study are equal to those obtained by Ullman and others (1971), who used the same dosage schedule. Thus most patients can be relied upon to take the second dose. The results are equal to those obtained by Svindland (1973) and Csonka (1969) who gave T-S for 2 to 5 days. They are better than those reported by Kvorning (1969), who used a 1-day treatment of trimethoprim 500 mg. and sulphamethoxazole 2,500 mg. The present trial confirms the good results using pivampicillin combined with probenecid reported by Malmborg, Molin, and Nyström (1973) and by Forström (1974).

Treatment of rectal gonorrhoea in women did not present any problem. No failures were observed in either of the two groups.

Tonsillar gonorrhoea has been reported to be less sensitive to ordinary anti-gonorrhoeal therapy. From and Veien (1974) reported a failure rate of approximately 50 per cent. in patients treated for tonsillar gonorrhoea with pivampicillin 1·4 g. combined with probenecid 1 g. or sulphamethoxazole 4 g. and trimethoprim 800 mg. as a 1-day treatment. However, both methods of treatment were effective if administered daily for 5 days. Ödegaard and Gundersen (1973) found a failure rate of 47 per cent. when treating gonococcal pharyngeal infections with ampicillin 2 g. combined with probenecid 1 g. Approximately the same results were obtained by Bro-Jørgensen and Jensen (1973) when using an oral one-dose treatment with ampicillin or pivampicillin, or a single injection of benzyl penicillin 5 m.u. preceded by probenecid 1 g. Bro-Jørgensen and Jensen (1973) obtained the best results with T-S in divided doses for one week. When using two tablets three times a day, each tablet containing sulphamethoxazole 400 mg. and trimethoprim 80 mg., all but one (who admitted re-exposure) of 29 patients were cured. Our findings are similar to those of a previous study from Marselisborg Hospital using the one dose treatment of intramuscular penicillin 5 m.u. preceded by probenecid 1 g. (Kristensen, 1974). In the present study there were two failures among thirteen treated with P-P and none among nine treated with T-S. Although the number of patients are small, the results are better than in the above-mentioned reports.

Both treatments seem safe with few side-effects. No statistically significant reduction in the frequency of post-gonococcal urethritis in the T-S group was found in this study. Other authors have found a reduction when using treatment with T-S for 5 days (Evans and others, 1972).

Our findings confirm that the 1-day treatment with T-S is just as effective as a single dose of P-P in the treatment of uncomplicated genital gonorrhoea. In tonsillar gonorrhoea T-S treatment is possibly more effective.

T-S is the drug of choice when incubating syphilis is suspected (Svindland, 1973). This may be an important reason for preference of T-S today. Successful treatment with T-S may be related to the present low incidence of strains of gonococci resistant to sulphonamides (Amies, 1969). Whether T-S will remain potent remains to be seen. It is therefore important to monitor the sensitivity pattern in the population at regular intervals (Svindland, 1973). Such studies are in progress at our department.

Summary

419 patients with uncomplicated gonorrhoea were treated with sulphamethoxazole 4 g. combined with

trimethoprim 0·8 g. divided into two doses with an 8-hr interval. The failure rate was 1·9 per cent. Parallel with this trial, 319 patients received pivampicillin 1·4 g. combined with probenecid 1 g.; the failure rate was 0·9 per cent. Side-effects were few, four patients in the first group and one in the second group developing a rash. No recurrences were noted in nine patients treated for tonsillar gonorrhoea with the trimethoprim-sulphamethoxazole schedule, while two recurrences were found in thirteen patients treated with pivampicillin-probenecid. The frequency of post-gonococcal urethritis was 7·7 per cent. in the pivampicillin-probenecid group against 3·4 per cent. in the trimethoprim-sulphamethoxazole group, a difference which was not statistically significant.

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La triméthoprime-sulfaméthoxazole dans la gonococcie. Comparaison avec la pivampicilline associée au probénécide

SOMMAIRE

419 sujets atteints de gonococcie non compliquée furent traités par 4 g de sulfaméthoxazole associé à 0,8 g de triméthoprime donnés en deux doses a 8 heures d'intervalle. Le taux des échecs fut de 1,9 pour cent. Parallèlement à cet essai, 319 malades furent traités par 1,4 g de pivampicilline associée à 1 g de probénécide. Le taux des échecs fut de 0,9 pour cent. Les effets secondaires furent rares; une éruption fut observée chez quatre malades du premier groupe et chez un du second. On n'observa pas de rechute chez 9 malades traités par le schéma triméthoprime-sulfaméthoxazole pour une gonococcie amygdalienne alors qu'on en nota deux pour 13 malades traités par pivampicilline-probénécide. La fréquence des urétrites post-gonococciques fut de 7,7 pour cent dans le groupe pivampicilline-probénécide contre 3,4 pour cent dans le groupe triméthoprime-sulfaméthoxazole, différence statistiquement non significative.